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UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA – WESTERN DIVISION

NEUROGRAFIX, a California corporation; WASHINGTON RESEARCH FOUNDATION, a not-for-profit Washington corporation,

Plaintiffs,

vs.

SIEMENS MEDICAL SOLUTIONS USA, INC., a Delaware corporation; and SIEMENS AKTIENGESELLSCHAFT, a German Corporation,

Defendants.

Case No. 10-CV-1990 MRP (RZx)

[Assigned to The Honorable Mariana R. Pfaelzer]

EXPERT REPORT RELATED TO CONSTRUCTION OF DR. AARON FILLER, M.D., PH.D, FRCS

First Amended Complaint Filed: July 30, 2010

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I. SUMMARY OF OPINIONS.

1. This report sets forth my opinion regarding the following terms in U.S. Patent No. 5,560,360 (the "'360 patent"):

- Claim 54(a): Excitation and output arrangement means for exposing a region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted gradients;
- Claim 54(c): Processor means coupled to said excitation and output arrangement means for processing said outputs to generate data representative of the diffusion anisotropy of the selected structure;
- Claim 55(c): Processor means…for: i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy;
- Claim 64: Processor means is further for processing said data representative of the diffusion anisotropy of the selected

structure to produce a data set that describes the shape and position of the selected structure; and

- Claims 58, 61: said processor means is further for [calculating]/[determining] a further data set that describes the three dimensional shape and position of a segment of said [neural tissue]/[selected structure] by: [i] analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said [neural tissue]/[selected structure]; and [ii] based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure exhibiting anisotropic diffusion] to be described.

2. My opinion describes how a person having ordinary skill in the art would have understood the terms as they are used in the '360 patent. In particular, this report expresses my opinions as to how one of skill in the art would have understood the disclosure of the specification of the '360 patent, and what structures the specification discloses and clearly links to the specifically recited function of each of the foregoing means plus function claim terms.

3. I base my opinion on the intrinsic evidence of the '360 patent, including its prosecution history and provisional applications included in the file history. A complete list of the material I considered is listed in Exhibit

A. I also base my opinions on my comprehensive education, research, knowledge and experience of over 15 years.

II. INTRODUCTION.

4. I have been asked to provide my opinion regarding how a person having ordinary skill in the art at the time of the application for the '360 patent would understand the meaning of the following terms as they are used in the '360 patent:

- Claim 54(a): Excitation and output arrangement means for exposing a region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted gradients;
- Claim 54(c): Processor means coupled to said excitation and output arrangement means for processing said outputs to generate data representative of the diffusion anisotropy of the selected structure;
- Claim 55(c): Processor means…for: i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected

structure from other structures in the region that do not exhibit diffusion anisotropy;

- Claim 64: Processor means is further for processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure; and
- Claims 58, 61: said processor means is further for [calculating]/[determining] a further data set that describes the three dimensional shape and position of a segment of said [neural tissue]/[selected structure] by: [i] analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said [neural tissue]/[selected structure]; and [ii] based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure exhibiting anisotropic diffusion] to be described.

5. It is my understanding that Defendants have proposed that all of the above terms are indefinite.

6. It is my understanding that NeuroGrafix has proposed the following constructions for each term:

Terms	Construction
Claim 54(a): Excitation and output arrangement means for exposing a	Function: exposing a region to a suppression sequence of

region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted gradients	electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted gradients Structures: 1. excitation coil 62 (also referred to RF excitation field coils, tuned RF excitation coils, phased array coils and phased array RF coil system in the specification); 2. RF pulse generator 84; 3. computer 72 and front-end circuit 74; and 4. their equivalents
Claim 54(c): Processor means coupled to said excitation and output arrangement means for processing said outputs to generate data representative of the diffusion anisotropy of the selected structure	Function: processing said outputs to generate data representative of the diffusion anisotropy of the selected structure Structures: 1. computer 72 and front-end circuit 74; 2. host processing system 32; and 3. their equivalents
Claim 55(c): Processor means…for: i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in	Function: i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region,

the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy	said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy Structures: 1. computer 72 and front-end circuit 74; 2. host processing system 32; and 3. their equivalents
Claim 64: Processor means is further for processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure	Function: processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure Structures: 1. computer 72 and front-end circuit 74; 2. host processing system 32; and 3. their equivalents
Claims 58, 61: said processor means is further for [calculating]/[determining] a further data set that describes the three dimensional shape and position of a segment of said [neural tissue]/[selected structure] by: [i] analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said [neural tissue]/[selected structure]; and [ii] based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure	Function: [calculating]/[determining] a further data set that describes the three dimensional shape and position of a segment of said [neural tissue]/[selected structure] by: [i] analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said [neural tissue]/[selected structure]; and [ii] based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure exhibiting anisotropic diffusion] to be described

exhibiting anisotropic diffusion] to be described	Structures: 1. computer 72 and front-end circuit 74; 2. host processing system 32; and 3. their equivalents

7. A complete list of the materials I have considered in determining my opinions is contained in Exhibit A to my report.

III. QUALIFICATIONS.

8. I hold a BA (biology 1977), MA (anthropology 1979) and an MD (1986) from the University of Chicago and a PhD (anthropology 1986) from Harvard University. My BA thesis dealt with principal component and eigenvector analysis of cranial anatomy and my MA thesis and PhD thesis dealt with spinal anatomy and its neurological basis. I have completed an 8-year residency in neurosurgery at the University of Washington, followed by a one-year neuroimaging fellowship in the U.K., then additional fellowships in spinal surgery and peripheral nerve surgery.

9. I am the author of more than two-dozen academic book chapters and peer reviewed scientific publications in the field of neuroimaging. These articles have been published in journals such as "Radiology," "Magnetic Resonance in Medicine" and "Journal Of Magnetic Resonance Imaging." Among my most recent peer reviewed publications are ones in which I outline the mathematical basis for an antisymmetric dyadic tensor model for vector processed neural tract images and in which I describe experimental work on the use of advanced imaging technology to assess biochemical events in nerve axons.

10. I also practice neural imaging on a regular basis. I have done so for the last 15 years. I regularly research and develop new pulse sequences for imaging nerves. In clinical practice, I have read and prepared interpretations on more than 10,000 neural images of various types. I also have an understanding of how MRI machines operate, both in a basic sense as well as in the particular use of imaging nerves. I have actually built handmade MRI hardware for use in advanced MRI imaging studies.

11. I have been an invited speaker at more than 75 scientific meetings in the United States, Europe and China and have made more than 75 scientific technical presentations at academic society meetings related to neuroimaging – including presentations at the annual meetings of the American Society for Neuroradiology and Radiological Society of North America. I recently served as the Session Chairman for an international meeting on Magnetic Resonance Imaging held in Singapore. I have lectured about MRI hardware and software as a Visiting Professor at Harvard University. My most recent lecture on MRI spatial resolution and image accuracy was presented at the Interventional MRI Symposium in Leipzig, Germany in September of 2010.

12. I am the section editor for the Peripheral Nerve section of the forthcoming 6th edition of the principal textbook in neurosurgery (Youmans Neurological Surgery) in which there are 18 chapters dealing with various aspects of peripheral nerve pathology and treatment. I am also the author of the chapter on nerve imaging in the forthcoming edition of the other major textbook in neurosurgery – Schmidek and Sweet – Operative Neurosurgical Techniques. I also serve as a peer reviewer for several academic journals including NeuroImage, Neurosurgery, Journal of Neurological Sciences, and PLOS ONE.

13. I am the inventor on 10 granted US Patents in a variety of fields including MRI hardware, neural drug delivery, and DNA technology.

14. I am the author of a 1,000 page technical book about computer microprocessors, machine language, peripherals and software (Apple Thesaurus, Datamost 1984); a technical book about spinal anatomy (Axial Character Seriation in Mammals, a republication of my Harvard Ph.D thesis); a general book on spine care (Do You Really Need Back Surgery – Oxford University Press 2004, 2007) and a book on evolutionary theory (Upright Ape – Career Press 2007 – with a foreword by David Pilbeam, Dean of Harvard College).

15. I have been retained as a qualified expert witness in more than 45 court cases in the past 15 years. In 39 of those cases, the testimony concerned neural imaging.

16. I am a former Commander (Lieutenant Colonel) of the 1466th Neurosurgical Medical Detachment (US Army Reserve), have served on the faculty of UCLA and University of London, have served as a Medical Director at Cedars Sinai Hospital in Los Angeles, and have taught for five years at Harvard University. I have also served as CEO or Chief Scientific Officer of several corporations.

17. My resume is attached as Exhibit B to this report.

IV. PERSON HAVING ORDINARY SKILL IN THE ART.

18. I am informed that, at this time, NeuroGrafix believes that a person having ordinary skill in the art for the '360 patent is a medical doctor with an M.D., three years of residency and a 1 year fellowship in neuroradiology or musculoskeletal radiology and at least 2 years experience in neuroradiology or musculoskeletal radiology, or equivalent education and experience in neuroradiology or musculoskeletal radiology. A person having ordinary

skill in the art will also have substantial experience (*e.g.*, 2 years) designing or studying MRI machines.

V. UNDERSTANDING OF THE LAW.

19. I have been informed and understand that claim construction is the process of determining the meaning of a term used in a patent claim. I have also been informed and understand that the proper construction of a claim term is generally the meaning that a person having ordinary skill in the art (*i.e.*, the technical field to which the patent relates) would have given to that term at the time when the patent's application was filed.

20. I understand that, for claim construction, one must focus on the claim terms in the context of the claim as a whole, interpreting the claim language as it ordinarily would be understood. After the claim language, the most important sources to consider are the patent specification, including any publications incorporated by reference in the specification, and the prosecution history. I understand that, collectively, these sources—the claim language, specification, and prosecution history—are called "intrinsic evidence."

21. In addition, it is my understanding that the Court may consider dictionaries, technical references, and other information—called "extrinsic evidence"—that would have been available at the time the patent's application was filed. I understand that the law requires that extrinsic evidence not be used to contradict claim meaning that is unambiguous in light of the intrinsic evidence.

22. It is my understanding that some claims terms are written in a special form, called "means plus function." It is my understanding that the construction of a means plus function claim term is a two-step process. First, the function of the means plus function claim term must be identified.

Second, one must identify what structures disclosed in the specification are clearly linked to the specifically recited function. If the specification fails to clearly link the recited functionality to a structure, it is indefinite.

VI. MY OPINIONS.

23. My full opinions regarding the terms below are detailed below. This report is written in two parts. The first part contains a brief introduction to what MRI is and how MRI works. Because one of skill in the art would have this knowledge, and because the claim construction interprets the specification and the claims from the viewpoint of one of skill in the art, I hope this background will be useful to the Court. The second part addresses several of the particular terms at issue and sets forth my opinions as to what structures one of skill would understand the specification to disclose and clearly link to the recited functions for the various disputed means plus function claim terms.

A. Brief Introduction To The Operation Of An MRI Machine.

24. The specification provides a background in the basic functionality of an MRI machine as well as the basic physical properties of certain tissues and fluids that are necessary to understand the invention. In order to fully understand how a person having ordinary skill in the art would understand the claims and the disclosure in the specification, I provide the following summary of the background section as well as supplemental background information that is known by one having ordinary skill in the art.

25. Magnetic Resonance Imaging (MRI) is a more elaborate version of Nuclear Magnetic Resonance (NMR). To understand the function and components of an MRI machine, it is helpful to first consider how NMR works. The fundamental difference between NMR and MRI is that NMR measures magnetic resonance phenomena in a single sample volume, while

MRI runs the NMR measurement hundreds of times for a structured set of hundreds of separate small volumes throughout the imaging subject.

1. Basics of Nuclear Magnetic Resonance (NMR).

a) The polarizing main field.

26. In NMR, a strong polarizing magnetic field is applied to a sample to gain control of and to coordinate the magnetic spins of the atomic nuclei in the sample, such as a person's arm or leg. Because protons have a positive charge and because they spin on their axis, each proton generates a tiny magnetic moment perpendicular to the direction of its spin.

27. Applying an external magnetic field assures that the magnetic axis of all of the protons in the sample are perfectly aligned with each other, parallel to the magnetic flux lines of the polarizing field.

28. The polarizing main field is typically applied by main polarizing field coils or the like.[1]

b) The phase coherence of the spins.

29. The rate at which a proton spins is determined by the strength of the external magnetic field. For instance, at 4.7 Tesla (a very powerful magnetic field), the protons all spin at exactly 200 megahertz (MHz) – 200 million cycles per second.

30. Conveniently, a spin rate of 200 megahertz is in the range of a radio signal. If we set a radiofrequency (RF) transmitter to output a signal at exactly 200 MHz, pumping this RF signal into the sample in the 4.7T NMR machine will allow the signal to deposit its oscillating energy at exactly the As we adjust the RF signal closer and closer to 200 MHz, the intrinsic resonant frequency of the protons in this example, the RF signal becomes

[1] The main polarizing field is discussed, for example, at column 2, lines 10 through 18 of the '360 patent.

capable of pumping additional coherent energy into the protons in the sample.

31. The RF transmitter can also be called RF coils or similar names. The RF signal is often known as an excitation field.

32. Once the transmitter is tuned to exactly the 200 MHz set by the external applied polarizing field, two things happen to the protons in the sample. Firstly, all of the protons begin to spin in phase with each other. Secondly, since they cannot spin any faster, they begin to tip like a spinning top leaning off vertical. In addition to spinning on their central axis, that axis is tipped and precesses around the original axis.

33. The amount of energy pumped into the sample can be carefully controlled by adjusting the strength of the applied RF signal and the duration. If it is set just right, it will tip all the protons by 90 degrees so that the axis of each proton is nearly perpendicular to the main field.[2]

c) Listening to the protons.

34. Once the excitation field causes all of the protons to be pumped into phase with each other and tipped so that thousands of proton axes are precessing around in perfect phase with each other, the RF transmitter is turned off and an antenna is used to detect the RF signal output from the sample at 200 MHz.

35. As long as the protons are tipped by even a few degrees, they will output a radio signal as they spin around. With the RF transmitter (and therefore the excitation field) turned off, the protons will gradually lose their extra energy and slowly return to vertical alignment in the main polarizing field. When they reach vertical, they will no longer emit any RF signal. The

[2] The rf excitation field is discussed, for example, at column 2, lines 19 through 67.

signal is strongest when they are tipped 90 degrees to a horizontal position and goes back down to zero when they are vertical again (aligned with the main polarizing field).

36. The slow loss of signal as they come back to vertical is called the T1 decay time. The emitted signal is called an echo.

37. The detection of the RF output from the proton can be called the "sensing of the resonant response."

38. The antenna is often called an antenna or an output or return coil. The antenna can also be combined with the RF transmitter, which can also be an antenna, to perform both the excitation and sensing functions. Where the RF transmitter and receiving antenna are combined, a control computer instructs the antenna to initiate the excitation field. The same computer, as the next step, switches the antenna to be connected to a radio receiver that hears the incoming, slowly decaying 200 MHz echo signal from the sample.[3]

d) T2 decay.

39. Some other physical factors affect the decay rate. Once the excitation RF signal is turned off, the magnetic fields of each of the spinning protons interact with each other causing tiny increases and decreases in the spin rate. The effect of this is that the sample as a whole loses phase coherence. As the protons begin to lose their phase coherence, the signal begins to decay away. This sort of decay due to "spin-spin" interactions is called the T2 decay.

40. The physical properties of the molecules and the surroundings in different tissues in the body cause different T1 and T2 decay rates for different tissues. These different properties allow NMR sequences to be

[3] The sensing of the output and T1 decay is discussed, for example, in column 2, lines 31 through 49.

developed that selectively emphasize or deemphasize certain types of tissues and fluids.[4]

2. MRI is based on location gradients.

41. The basic idea of MRI as opposed to simple NMR is to do an NMR experiment hundreds of times so that the NMR signal properties (and hence the chemical composition) of hundreds of different locations can be measured. Spatial control allows an MRI operator to selectively listen to just the tissue, or region of tissue, that is of interest.

a) Locational gradients.

42. This problem of spatial control was solved in the early 1970s by Paul Lauterbur who won the Nobel Prize for his part in the invention of MRI. He applied a second magnetic field in addition to the main polarizing field. However, instead of a uniform field throughout the sample volume, this second field had a gradient, meaning that the strength of the field varied across the field. Thus, for example, the polarizing field would be 4.69 Tesla on the left, 4.70 Tesla in the center and 4.71 Tesla on the right. Thus, water protons on the left would have a resonant frequency of (for a simplified example) 199 MHz, in the center they would be at 200 MHz and to the right they would have a frequency of 201 MHz. This second field has become known as a gradient field and is also referred to as the spatial or locational gradient field.

43. The gradient field can be used to excite and sense protons in specific areas. For example, using the frequencies in the above paragraph, the RF transmitter could be tuned to 199 MHz and stimulate only the water on the

[4] T2 decay is discussed, for example, in column 2, lines 40 through 49.

left. Thus, any output received would only be for the tissue on the left side of the sample.

44. In an MRI machine, one or more gradient coils generate the gradient field.

45. In practice, it becomes possible to apply three different gradients along the three main axes of three-dimensional (Cartesian) space (X is up and down, Y is left to right, and Z is along the length of the person). Gradient fields in these axes allow MRI machines to have a unique field strength for each spot in the body. Therefore, by precise tuning, it is possible to listen to any location within the sample. An MRI machine can use this functionality to sense output from each of hundreds of locations from the body.[5]

46. Each individual output of a targeted location in the body is often called a "slice."

47. Using a series of activations of the locational gradients and a series of events of excitation (*e.g.*, RF signals from RF coils) and sensing at a given echo time, it is possible to collect intensities from each point in the selected slice. Depending on the quality of the electronics used in the MRI machine, it is possible for example to separately address and measure 256 different locations from right to left and 256 locations from top to bottom. The result is a 256 x 256 pixel image with a different brightness in each pixel. This is often referred to as an assembled MRI cross sectional image.

3. Control and Computation in an MRI.

48. The operation of an MRI machine involves the activation of a "pulse sequence." A exemplary drawing of a pulse sequence appears in Figure 11

[5] The use of locational gradients is discussed, for example, at column 3, lines 1 through 23.

of the 5,560,360 patent. A pulse sequence defines the sequence of events to be used to sense a particular region with a particular configuration. This includes the application of the main polarizing field, one or more gradient fields, one or more excitation fields and an output sensing time.

49. The sequence must then be repeated hundreds of times. Time is allowed between each repetition of the pulse sequence to allow protons to return as completely as possible to the vertical before the next rendition of the pulse sequence is run. This is the repetition time (TR).

50. The pulse sequences, including the manipulation of the RF coils, output coils or antenna, main polarizing coils and gradient coils, are all controlled by one or more computers and front-end circuits. The MRI machine is configured through this hardware by its operator.

51. Furthermore, the computers and front-end circuits used by an MRI machine are also used to process the output received as a result of the pulse sequences. In MRI machines, such analysis includes converting the data received by the antenna into two- and three-dimensional images of the regions of interest as well as other processing that might be required by the particular application sought.[6]

4. Use of Diffusion in NMR and MRI.

52. Although Diffusion MRI is a particular application of an MRI machine, I provide a basic background of its operation because it is helpful to understanding the specification and the context with which one having ordinary skill in the art would read it.

[6] The control of an MRI machine using pulse sequences and the processing of the resulting output is discussed throughout the patent, including at column 3, lines 24 though 34 and column 11, lines 9 through 18 and lines 28 through 49.

53. Diffusion is the movement of the water proton as it decays after the application of the excitation field. Through the use of gradients, this diffusion movement can be measured.

54. In a liquid such as spinal fluid that resembles clear water, diffusion of water molecules takes place uniformly in all directions. This is called isotropic diffusion. However, in a few tissues in the body such as nerve and muscle, diffusion takes place preferentially along specific directions. In nerve, water diffuses more rapidly along the length of the nerve then it does going crossways from one side of the nerve axon to the other. This directional diffusion is called anisotropic diffusion.[7]

55. Gradients can be used to image tissues that exhibit diffusion anisotropy and distinguish them from tissues that exhibit isotropic diffusion. If the gradient is directed perpendicular to the nerve, the isotropically diffusing water will decay at a rate related to the typical diffusion rate in that tissue and the tissues around it. However, the water molecules diffusing anisotropically up and down the length of the nerve will be staying in the same gradient strength and will not be subject to decay from their diffusion motion. If the gradient is now turned parallel to the nerve, the isotropically diffusing water will decay at exactly the same rate as before. However, the water diffusing up and down the length of the nerve will be moving rapidly to new positions in the gradient and will be subject to decay at even faster rates than the isotropic water. In the nerve-perpendicular image, the nerve will appear relatively bright relative to background, and in the nerve-parallel image the nerve will appear relatively dark.[8]

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[7] Anisotropic diffusion is sometimes also referred to as restricted diffusion.

[8] Diffusion MRI is discussed, for example, at column 5, lines 13 through 65.

56. With this background, I now turn to the claims terms I have been asked to address.

B. Specific Disputed Means Plus Function Terms

1. Claim 54(a): Excitation and output arrangement means for exposing a region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted gradients

57. A person having ordinary skill in the art at the time of the invention would have understood that the recited functionality is: "exposing a region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted gradients."

58. A suppression sequence in the context of this claim language refers to a sequence of electromagnetic pulses or, in other words, a "pulse sequence."

59. The recited function thus requires exposing a region to a pulse sequence (sequence of electromagnetic fields) that suppresses the responsiveness of structures do not exhibit diffusion anisotropy (that is, structures that are isotropic). The specification expressly discloses at least

two examples of isotropic tissues or fluids: fat ('360 patent at 5:60-61 ("fat is isotropic")) and short T2 isotropically diffusing water ('360 patent 28:36-37). A person having ordinary skill in the art at the time of the invention would also have known that other tissues (such as bone or liver) and fluids, such as blood in blood vessels, are also isotropic.

60. Using a pulse sequence that suppresses fat (a tissue that does not exhibit anisotropy) is referred to in the patent as fat suppression. *See, e.g.*, '360 patent 13:7-31, Fig. 12.

61. The specification discloses that fat suppression increases the "apparent magnitude of diffusion anisotropy." *See* 13:3-6; 22:28-23:26. The specification, when viewed by a person having ordinary skill in the art, clearly discloses that a fat suppression pulse sequence is an example of the recited functionality of exposing a region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-weighted gradients. *See, e.g.*, '360 patent at 12:64-13:48.

62. The specification discloses and expressly links the excitation coil 62 (also referred to RF excitation field coils, tuned RF excitation coils, phased array coils and phased array RF coil system in the specification), RF pulse generator 84, and computer 72 and front-end circuit 74 as the structures that perform the specifically recited functionality.

63. One example of fat suppression described in the specification is chemical shift selective (CHESS). '360 patent at 13:7-24. CHESS does not use diffusion-weighted gradients. *See, e.g.*, Haase et al., *H NMR Chemical*

Shift Selective (CHESS) Imaging, Phys. Med. Biol. 341-344 (Vol. 30, No. 4 1985). Exposing a region to the CHESS pulse sequence is therefore an example of the recited function because it (1) suppresses responsiveness of structures that do not exhibit diffusional anisotropy (*e.g.*, fat), which in turn (2) increases the "apparent magnitude of diffusional anisotropy (*e.g.*, '360 patent at 13:3-6), and (3) does not use diffusion-weighted gradients (*see, e.g.*, Haase et al., *H NMR Chemical Shift Selective (CHESS) Imaging*, Phys. Med. Biol. 341-344 (Vol. 30, No. 4 1985)).

64. The specification also expressly describes alternative fat suppression pulse sequences that are also examples of the recited function:

> "Other suitable alternatives include the Dixon technique for fat suppression described in, for example, Dixon et al., Simple Proton Spectroscopic Imaging, 153 RADIOLOGY 189-194 (1984) and also STIR (short tau inversion recovery) described in Improved Fat Suppression in STIR MR Imaging: Selecting Inversion Time through Spectral Display, 178 RADIOLOGY 885-887 (1991)."

'360 patent at 13:34-40. Those having ordinary skill in the art would understand that this is disclosing additional pulse sequences and further describing that these sequences suppress fat (*i.e.*, tissue not exhibiting anisotropy) thereby enhancing nerve and other tissues that exhibit anisotropy.

65. The specification expressly discloses that CHESS "involves the application of a sequence of narrow band rf pulses A, B and C to the excitation coil 62 to selectively excite the nuclear spins of fat molecules within the region R of the patient being imaged." '360 patent at 13:12-15; *see also* Fig. 11A. The specification clearly discloses that excitation coil 62 is pulsed by RF pulse generator 84 ('360 patent at 11:28-30 ("rf pulse

generator 84, which produces rf pulses")) and controlled by computer 72 and front-end circuit 74 ('360 patent at 11:11-14 ("Computer 72 and circuit 74 cooperatively control and synchronize the operation of MRI system 14")).

66. The specification therefore discloses and expressly links the following corresponding structures – excitation coil 62 (also referred to RF excitation field coils, tuned RF excitation coils, phased array coils and phased array RF coil system in the specification), RF pulse generator 84 and computer 72 and front-end circuit 74 – with the recited functionality of exposing a region to a suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion anisotropy (*e.g.*, fat), so as to increase the apparent diffusion anisotropy of structures in the region that exhibit diffusion anisotropy (*see* '360 patent at 13:3-6 ("apparent magnitude of diffusion anisotropy.")), said suppression sequence of electromagnetic fields not including diffusion-weighted gradients.[9]

2. Claim 54(c): Processor means coupled to said excitation and output arrangement means for processing said outputs to generate data representative of the diffusion anisotropy of the selected structure

67. A person having ordinary skill in the art at the time of the invention would have understood that the recited functionality is: "processing said outputs to generate data representative of the diffusion anisotropy of the selected structure."

[9] This is consistent with the disclosure on page 16 of provisional application no. GB 9216383, filed July 31, 1992.

68. The phrase "said outputs" in the recited functionality refers to the output indicative of the resonance response to each diffusion-weighted gradient in element (b) of claim 54.

69. The specification describes using "echo processing" as an example of processing the outputs to generate so called diffusion coefficients, which are data representing the diffusional anisotropy of the selected tissue or fluid (*e.g.*, a nerve). Echo processing refers to the processing of the received output indicative of the resonant response referred to in element (b) of claim 54. *See* '360 patent at 14:32-15:31.

70. The specification discloses that "for each of the different diffusional gradients employed, the spin-echo sequence is repeated, followed by the generation of image data and the processing of that data to, for example, quantify the relaxation time T_2 or diffusion coefficient D." '360 patent at 17:18-22.

71. The diffusional coefficients are representative of the diffusional anisotropy of the fluid or tissue being imaged. *See* '360 patent at 18:30-33 ("These coefficients provide a measure, associated with each pixel or voxel, of the magnitude of diffusional anisotropy at that point, while the anisotropic direction is indicated by the gradient orientation.").

72. The specification further discloses that "[t]he echo F produced using the diffusion weighted pulse echo sequence is processed in the manner described above in connection with blocks 112 through 128 of FIGS. 9 and 10. With diffusion weighting, the computation of the diffusional coefficient D at block 128 is preferably based upon the analysis of data collected for different gradient magnitudes." '360 patent at 18:8-13; *see also* '360 patent at 18:24-26 ("Once computer 72 determines, at block 130, that images have

been collected for all of the desired diffusional gradients, operation proceeds to block 150.").

73. Thus, echo processing of the outputs to calculate diffusion coefficients is an example of the recited functionality of processing said outputs to generate data representative of the diffusion anisotropy of the selected structure.

74. The specification discloses and clearly links computer 72 and front-end circuit 74 as the structure that performs the specifically recited functionality. Computer 72 and front-end circuit 74, as shown in Figure 8, encompass the processing system 16, input system 18, and output/display system 20 shown in Figure 6. '360 patent at 11:9-11.

75. The specification discloses an exemplary algorithm for performing the recited functionality. The algorithm is shown in Figures 9 and 10 and the portions of the specification describing Figures 9 and 1. Specifically, processing the outputs to generate the diffusion coefficient is shown in blocks 112 through 128 of figures 9 and 10 of the '360 patent and described in the accompanying text at column 14, line 33 through column 15, line 31. The calculation of diffusion coefficient D is well known to one having ordinary skill in the art. *See, e.g.*, Howe et al., *Magnetic Resonance Neurography*, Magnetic Resonance in Medicine 328-338 (1992); Le Bihan et al., *MR Imaging of Intravoxel Incoherent Motions: Application to Diffusion and Perfusion in Neurologic Disorders*, Radiology 161:401-407 (1986); Moseley et al., *Anisotropy in Diffusion-Weighted MRI*, 19 Magnetic Resonance on Medicine 321-326 (1991); *see also* 14:63-15:31.

76. The specification expressly discloses that "[c]omputer 72 and front-end circuit 74 ***cooperatively*** control and synchronize the operation of the MRI system 14, as well as process and display the acquired data." '360

patent at 11:11-14 (emphasis added). The specification further discloses that "[t]he computer 72 processes the resultant digital inputs, which represent the response of the spins to the applied fields, to generate the desired neurograms." '360 patent at 11:46-49; *see also* '360 patent at 8:54-57 ("the processing system 16 responds to operator inputs applied via input system 18 to control MRI system 14 and process its output to display the resultant neurograms at system 20.").

77. Echo processing, which is expressly described functionality in the specification, is an example of processing the output from the MRI system. The specification expressly and clearly links computer 72 and front-end circuit 74 to processing the output from the MRI system. *See, e.g.*, '360 patent at 11:11-14, 8:54-57.

78. Therefore, the specification, when viewed by a person having ordinary skill in the art, discloses and clearly links computer 72 and front-end circuit 74 to the recited functionality of processing said outputs to generate data representative of the diffusion anisotropy of the selected structure.

79. The fact that computer 72 and front-end circuit 74 were the standard processing structure used by MRI machines well known at the time of the invention is consistent with and supports the discussion above.

80. The specification also discloses and expressly links host processing system 32 to the recited functionality by indicating that host processing system 32 can be used in place of computer 72 and front-end circuit 74:

> "As one final component, medical system 12 may include a host processing system 32 in addition to, or in place of, separate processing systems in the other components of system 12."

'360 patent at 9:42-45.

81. Therefore, the specification, when viewed by one having ordinary skill in the art, discloses and clearly links computer 72 and front-end circuit 74, and host processing system 32 with the recited functionality of processing said outputs to generate data representative of the diffusion anisotropy of the selected structure.

3. Claim 55(c): Processor means…for: i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy

82. A person having ordinary skill in the art at the time of the invention would have understood that the recited functionality is: "i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy."

83. The phrase "said outputs" in the recited functionality refers to the output indicative of the resonant response to each diffusion-weighted gradient in element (b)(ii) of claim 55.

84. The recited functionality has two recited subfunctionalities. Recited subfunctionality 1 is "vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure." Recited subfunctionality 2 is "processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy."

a) Recited Subfunctionality 1: vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure

85. The specification clearly discloses an example of the vector processing in recited subfunctionality 1. The specification discloses that "a technique has been developed for observing diffusional anisotropy, independent of its degree of alignment with any individual gradient axes." '360 patent at 20:26-28. One of the examples used in the specification is a "vector analysis…used to produce interpolated images and directional information from the three orthogonal diffusion-weighted images described

above." '360 patent at 20:31-34. The directional information recited in the specification is the "data representative of anisotropic diffusion exhibited by a selected structure in the region" functionality disclosed in recited subfunctionality 1.

86. In fact, the entire section of the specification found at column 19, line 28 to column 22, line 27 is entitled "Vector Processing and Three-Dimensional Image Generation" and describes the use of vector processing of outputs to generate data representative of anisotropic diffusion. Column 20, line 25 to column 22, line 27 specifically discloses the functionality of vector processing outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure.

87. The specification discloses and expressly links recited subfunctionality 1 to computer 72 and front-end circuit 74 as the structure that performs recited subfunctionality 1. "The computer 72 is readily able to identify nerve locations in the anatomical structure and to correctly trace the course of the nerves between two-dimensional image planes or through a three-dimensional acquisition volume." '360 patent at 21:60-63; *see also* '360 patent at 20:24-25 ("As a preferred alternative, requiring less mechanical complexity and ***faster processing speed***" (emphasis added)). The specification also discloses that "[c]omputer 72 and front-end circuit 74 ***cooperatively*** control and synchronize the operation of the MRI system 14, as well as process and display the acquired data." '360 patent at 11:11-14 (emphasis added). Thus, the specification, as viewed by one having ordinary skill in the art, clearly links computer 72 and front-end circuit 74 to recited subfunctionality 1.

88. The specification also discloses examples of algorithms for performing recited subfunctionality 1:

- Using equations (3), (4), (5) and (6) to perform recited subfunctionality 1. *See, e.g.*, '360 patent at 20:46-21:15;
- Using arctan. *See, e.g.*, '360 patent at 21:16-23;
- Using the vector analysis described in Basser et al., *Fiber Orientation Mapping in an Anisotropic Medium with NMR Diffusion Spectroscopy*, SMRM BOOK OF ABSTRACTS 1221 (1992). *See, e.g.*, '360 patent at 21:36-38;
- Using the tensor analysis employing tensors of various ranks, described in Basser et al., *Diagonal and Off Diagonal Components of the Self-Diffusion Tensor: Their Relation to an Estimation from the NMR Spin-Echo Signal*, SMRM BOOK OF ABSTRACTS 1222 (1992). *See* '360 patent at 21:39-45; and
- Using alternative processing technical used in the evaluation of magnetic, thermal and structural anisotropy data. *See* '360 patent at 21:45-47.

89. The fact that computer 72 and front-end circuit 74 were the standard processing structure used by MRI machines well known at the time of the invention is consistent with and supports the discussion above.

90. The specification also discloses and expressly links host processing system 32 to the recited functionality by indicating that host processing system 32 can be used in place of computer 72 and front-end circuit 74:

> "As one final component, medical system 12 may include a host processing system 32 in addition to, or in place of, separate processing systems in the other components of system 12."

'360 patent at 9:42-45.

91. Therefore, the specification, when viewed by one having ordinary skill in the art, discloses and clearly links computer 72 and front-end circuit 74, and host processing system 32 with recited subfunctionality 1.

b) Recited Subfunctionality 2: processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy.

92. The specification clearly discloses an example of the processing in recited subfunctionality 2. The specification discloses that "computer 72 is readily able to identify nerve locations in the anatomical structure and to correctly trace the course of the nerves between two-dimensional image planes or through a three-dimensional acquisition volume." '360 patent at 21:51-54. The identification of locations and tracing the course of nerves are the shape and position of the selected tissue or fluid (*i.e.*, the nerve). Because the data was generated using diffusion-weighted gradients (*see* element (b) of claim 55), the resulting data will distinguish the nerve from other structures in the region that do not exhibit diffusion anisotropy, such as fat ('360 patent at 5:60-61 ("fat is isotropic")) and short T2 isotropically diffusing water ('360 patent 28:36-37). *See, e.g.*, '360 patent at Figs. 16, 17 (images resulting from this functionality showing the nerve distinguished from fluid and tissue that does not exhibit diffusion anisotropy); 5:3-30 (describing prior art use of diffusion-weighted gradients to distinguish anisotropic white matter tracks in the brain from isotropic matter).

93. The specification also discloses an algorithm to perform recited subfunctionality 2: "For example, the location of nerves in a given image plane can be detected by comparing pixel intensity to some threshold level. A three-dimensional image can then be formed by linking or projecting the results of these two-dimensional analyses over the desired volume." '360 patent at 21:55-59.

94. The specification also discloses an alternative algorithm to perform recited subfunctionality 2 by tracking continuous serial changes in the direction of maximum anisotropy for the nerve. '360 patent at 21:60-22:5. The specification also discloses an alternative algorithm to perform recited subfunctionality 2 by using a "three dimensional" imaging sequence and generating a subtraction angiogram. '360 patent at 22:6-17.

95. The specification discloses and expressly links recited subfunctionality 2 to computer 72 and front-end circuit 74 as the structure that performs recited subfunctionality 2. '360 patent at 21:60-31 ("The computer 72 is readily able…"). The specification also discloses that "[c]omputer 72 and front-end circuit 74 ***cooperatively*** control and synchronize the operation of the MRI system 14, as well as process and display the acquired data." '360 patent at 11:11-14 (emphasis added). Thus, the specification, as viewed by one having ordinary skill in the art, clearly links computer 72 and front-end circuit 74 to recited subfunctionality 2.

96. The fact that computer 72 and front-end circuit 74 were the standard processing structure used by MRI machines well known at the time of the invention is consistent with and supports the discussion above.

97. The specification also discloses and expressly links host processing system 32 to the recited functionality by indicating that host processing system 32 can be used in place of computer 72 and front-end circuit 74:

> "As one final component, medical system 12 may include a host processing system 32 in addition to, or in place of, separate processing systems in the other components of system 12."

'360 patent at 9:42-45.

98. Therefore, the specification, when viewed by one having ordinary skill in the art, discloses and clearly links computer 72 and front-end circuit 74, and host processing system 32 with recited subfunctionality 2.

99. In summary, as shown above, the specification, when viewed by one having ordinary skill in the art, discloses and clearly links computer 72 and front-end circuit 74, and host processing system 32 with the recited functionality of element c of claim 55: "i) vector processing said outputs to generate data representative of anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of said diffusion-weighted gradients with respect to the orientation of said selected structure; and ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy."

4. Claim 64: Processor means is further for processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure.

100. A person having ordinary skill in the art at the time of the invention would have understood that the recited functionality is: "processing said data representative of the diffusion anisotropy of the selected structure to

produce a data set that describes the shape and position of the selected structure."

101. The phrase "said data representative of the diffusion anisotropy of the selected structure" refers to the data generated in element (c) of claim 54, discussed above.

a) Subtraction processing.

102. The said data representative of the diffusion anisotropy of the selected structure is collected for each diffusion gradient. *E.g.*, '360 patent at 18:18:11-13, 18:24-26. If the axis of the anisotropy is unknown, the diffusional coefficient D for each diffusion gradient is compared to identify the minimum and maximum values. '360 patent at 18:26-30.

103. Once the images associated with the minimum and maximum diffusional coefficient D are identified, they are "mathematically (or photographically or optically) subtracted from one another" to produce a subtraction neurogram. '360 patent at 18:35-46. A subtraction neurogram "sharply highlights a nerve rather than a vessel." '360 patent at 18:53-55; *see also* 3:36-64 (discussing angiograms of blood vessels, which are similar to a subtraction neurogram).

104. A subtraction neurogram is "particularly useful for confirming the identification of nerves in a given imaging plane or space as well as for locating nerve injuries and nerve compressions." '360 patent at 56-58. In other words, subtraction neurograms perform the recited function of processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure.

105. The specification discloses performing an algorithm for creating a subtraction neurogram. '360 patent at Figs. 15B-15D, 18:35-46. The

specification also discloses an algorithm supplementing the subtraction process by dividing by the "signal information from a fat suppressed, T2-weighted spin echo sequence (e.g. using the aforementioned CHESS technique)." '360 patent at 19:2-7. The specification also describes an algorithm that uses a threshold analysis instead of subtraction. '360 patent at 18:67-19:2.

106. The specification discloses and expressly links the recited functionality to computer 72 and front-end circuit 74 as the structure that performs the recited functionality. The image selection/production process, which encompasses the subtraction processing recited functionality, is expressly being performed by computer 72. '360 patent at 18:24 ("Once computer 72 determines…"). The specification also discloses that "[c]omputer 72 and front-end circuit 74 ***cooperatively*** control and synchronize the operation of the MRI system 14, as well as process and display the acquired data." '360 patent at 11:11-14 (emphasis added). Thus, the specification, as viewed by one having ordinary skill in the art, clearly links computer 72 and front-end circuit 74 to the recited functionality of processing said data representative of the diffusion anisotropy of the selected structure (*e.g.*, a nerve) to produce a data set that describes the shape and position of the selected structure (*e.g.*, a subtraction neurogram).

107. The fact that computer 72 and front-end circuit 74 were the standard processing structure used by MRI machines well known at the time of the invention is consistent with and supports the discussion above.

108. The specification also discloses and expressly links host processing system 32 to the recited functionality by indicating that host processing system 32 can be used in place of computer 72 and front-end circuit 74:

> "As one final component, medical system 12 may include a host processing system 32 in addition to, or in place of, separate processing systems in the other components of system 12."

'360 patent at 9:42-45.

b) Vector processing.

109. The specification also discloses another method of performing the recited functionality of processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure.

110. The specification clearly discloses an example of the processing in the recited functionality. The specification discloses that "computer 72 is readily able to identify nerve locations in the anatomical structure and to correctly trace the course of the nerves between two-dimensional image planes or through a three-dimensional acquisition volume." '360 patent at 21:51-54. The identification of locations and tracing the course of nerves are the shape and position of the selected tissue or fluid (*i.e.*, the nerve).

111. The specification also discloses an algorithm to perform the recited functionality: "For example, the location of nerves in a given image plane can be detected by comparing pixel intensity to some threshold level. A three-dimensional image can then be formed by linking or projecting the results of these two-dimensional analyses over the desired volume." '360 patent at 21:55-59. The specification also discloses an alternative algorithm to perform the recited functionality by tracking continuous serial changes in the direction of maximum anisotropy for the nerve. '360 patent at 21:60-22:5.

112. The specification discloses and expressly links the recited functionality to computer 72 and front-end circuit 74 as the structure that

performs the recited functionality. '360 patent at 21:60-31 ("The computer 72 is readily able…"). The specification also discloses that "[c]omputer 72 and front-end circuit 74 ***cooperatively*** control and synchronize the operation of the MRI system 14, as well as process and display the acquired data." '360 patent at 11:11-14 (emphasis added). Thus, the specification, as viewed by one having ordinary skill in the art, clearly links computer 72 and front-end circuit 74 to the recited functionality of processing said data representative of the diffusion anisotropy of the selected structure (*e.g.*, a nerve) to produce a data set that describes the shape and position of the selected structure.

113. The fact that computer 72 and front-end circuit 74 were the standard processing structure used by MRI machines well known at the time of the invention is consistent with and supports the discussion above.

114. The specification also discloses and expressly links host processing system 32 to the recited functionality by indicating that host processing system 32 can be used in place of computer 72 and front-end circuit 74:

> "As one final component, medical system 12 may include a host processing system 32 in addition to, or in place of, separate processing systems in the other components of system 12."

'360 patent at 9:42-45.

115. Therefore, the specification, when viewed by one having ordinary skill in the art, discloses and clearly links computer 72 and front-end circuit 74, and host processing system 32 with the recited functionality of processing said data representative of the diffusion anisotropy of the selected structure (*e.g.*, a nerve) to produce a data set that describes the shape and position of the selected structure (*e.g.*, by using subtraction processing or vector processing).

5. Claims 58, 61: said processor means is further for [calculating]/[determining] a further data set that describes the three dimensional shape and position of a segment of said [neural tissue]/[selected structure] by: [i] analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said [neural tissue]/[selected structure]; and [ii] based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure exhibiting anisotropic diffusion] to be described.

116. It is my understanding that the parties agree the construction of this phrase as used in claim 58 will be the same as the construction of the phrase as used in claim 61.

117. It is further my understanding that both claim 58 and claim 61 ultimately depend on claim 55. Claim 61 directly depends on claim 55. Claim 58 depends on claim 55 via claim 56. Claim 56 claims that the selected structure in claim 55 is "neural tissue in a mammal" and the other structures in claim 55 are "non-neural tissue in the mammal."

118. A person having ordinary skill in the art at the time of the invention would have understood that the recited functionality is: "[i] analyzing the

data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said [neural tissue]/[selected structure]; and [ii] based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure exhibiting anisotropic diffusion] to be described."

119. "Said additional data sets…" refers to the "additional data sets describing different cross sections…" in the preamble of claims 58 and 61. The specification discloses that cross sections are two-dimensional images, as illustrated by Figures 20, 21 and 23. *See also* '360 patent at 8:17-22, 8:26-28 (describing figures), 12:7 ("two-dimensional cross section").

120. The specification describes the data sets referenced in the recited functionality where, among other places, it notes that, until the functionality described in these claims and claim 55, "the output produced is generally in the form of a single two-dimensional image, or a series of two-dimensional images that can be related to form a three-dimensional image" with a high signal to noise ratio (in other words, low accuracy). '360 patent at 19:30-38; *see also, e.g.*, '360 patent at 20:35-45 (describing example with "four 'multi-slice' sets").

121. The specification clearly discloses an example of the recited functionality. The specification discloses that the "computer 72 is readily able to identify nerve locations in the anatomical structure and to correctly trace the course of the nerves between two-dimensional image planes or through a three-dimensional acquisition

volume. For example, the location of nerves in a given image plane can be detected by comparing pixel intensity to some threshold level. A three-dimensional image can then be formed by linking or projecting the results of these two-dimensional analyses over the desired volume." '360 patent at 21:51-59. The analysis of image intensity and linking of the results into a three-dimensional image is an example of the recited functionality.

122. In fact, the entire section of the specification found at column 19, line 28 to column 22, line 27 is entitled "Vector Processing and Three-Dimensional Image Generation" and describes the use of vector processing of outputs to generate data representative of anisotropic diffusion. Column 20, line 25 to column 22, line 27 specifically discloses the functionality of vector processing outputs to generate a data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure exhibiting anisotropic diffusion] to be described.

123. The specification also discloses examples of algorithms for performing the recited functionality:

- Using equations (3), (4), (5) and (6) to perform recited subfunctionality 1. *See, e.g.*, '360 patent at 20:46-21:15;
- Using arctan. *See, e.g.*, '360 patent at 21:16-23;
- Using the vector analysis described in Basser et al., *Fiber Orientation Mapping in an Anisotropic Medium with NMR Diffusion Spectroscopy*, SMRM BOOK OF ABSTRACTS 1221 (1992). *See, e.g.*, '360 patent at 21:36-38;
- Using the tensor analysis employing tensors of various ranks, described in Basser et al., *Diagonal and Off Diagonal*

Components of the Self-Diffusion Tensor: Their Relation to an Estimation from the NMR Spin-Echo Signal, SMRM BOOK OF ABSTRACTS 1222 (1992). *See* '360 patent at 21:39-45; and

- Using alternative processing technical used in the evaluation of magnetic, thermal and structural anisotropy data. *See* '360 patent at 21:45-47.

124. The specification discloses and expressly links the recited functionality to computer 72 and front-end circuit 74 as the structure that performs the recited functionality. '360 patent at 21:60-31 ("The computer 72 is readily able…"). The specification also discloses that "[c]omputer 72 and front-end circuit 74 ***cooperatively*** control and synchronize the operation of the MRI system 14, as well as process and display the acquired data." '360 patent at 11:11-14 (emphasis added). Thus, the specification, as viewed by one having ordinary skill in the art, clearly links computer 72 and front-end circuit 74 to the recited functionality.

125. The fact that computer 72 and front-end circuit 74 were the standard processing structure used by MRI machines well known at the time of the invention is consistent with and supports the discussion above.

126. The specification also discloses and expressly links host processing system 32 to the recited functionality by indicating that host processing system 32 can be used in place of computer 72 and front-end circuit 74:

> "As one final component, medical system 12 may include a host processing system 32 in addition to, or in place of, separate processing systems in the other components of system 12."

'360 patent at 9:42-45.

127. Therefore, the specification, when viewed by one having ordinary skill in the art, discloses and clearly links computer 72 and front-end circuit

74, and host processing system 32 with the recited functionality of analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said [neural tissue]/[selected structure]; and based upon the results of said analyzing the data representative of anisotropic diffusion, combining said data set and said additional data sets to generate said further data set that describes the three dimensional shape and position of the segment of said [neural tissue]/[selected structure], thereby allowing a three dimensional shape and position of curved [neural tissue]/[structure exhibiting anisotropic diffusion] to be described.

I declare under penalty of perjury that the statements in this report are true and correct.

Executed on January 24, 2011 in Santa Monica, California.

Dr. Aaron Filler, M.D., Ph.D., FRCS

EXHIBIT A

Evidence Considered

U.S. Patent No. 5,560,360;

File History of U.S. Patent No. 5,560,360, including provisional applications included therein;

Haase et al., *H NMR Chemical Shift Selective (CHESS) Imaging*, Phys. Med. Biol. 341-344 (Vol. 30, No. 4 1985);

Howe et al., *Magnetic Resonance Neurography*, Magnetic Resonance in Medicine 328-338 (1992);

Le Bihan et al., *MR Imaging of Intravoxel Incoherent Motions: Application to Diffusion and Perfusion in Neurologic Disorders*, Radiology 161:401-407 (1986);

Moseley et al., *Anisotropy in Diffusion-Weighted MRI*, 19 Magnetic Resonance on Medicine 321-326 (1991);

Susumu Mori, Introduction to Diffusion Tensor Imaging (Elsevier 2007); and

My general knowledge and understanding.